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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/696,194	10/26/2000	Derek O'Hagan	1629.002	4102

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EXAMINER	
PARKIN, JEFFREY S	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 01/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/696,194	O'HAGAN ET AL.	
	Examiner	Art Unit	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *03* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-25,27,28 and 30-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-25,27,28,30,31,34 and 36-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

Status of the Claims

1. Claims 1, 3, 4, 10, 11, 14-19, 23, 24, and 28 were amended, claims 2, 26, and 29 canceled without prejudice or disclaimer, and new claims 32-43 submitted in the response dated 29 September, 2003. Accordingly, claims 1, 3-25, 27, 28, and 30-43 are currently under examination.

Information Disclosure Statement

2. The information disclosure statement filed 29 September, 2003, has been placed in the application file and the information referred to therein has been considered.

35 U.S.C. § 112, Second Paragraph

3. Amended claim 14 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim has been amended to recite "wherein the mucosal secretion is obtained from." which is vague and indefinite. Appropriate correction is required.

35 U.S.C. § 103(a)

4. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as

> prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

6. The factual inquiries set forth in *Graham et al. v. John Deere Company of Kansas City et al.; Calmar, Inc. v. Cook Chemical Company; Colgate-Palmolive Company v. Same*, 148 U.S.P.Q. 459 (U.S. Sup. Ct. 1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103 are summarized as follows: 1) Determining the scope and contents of the prior art. 2) Ascertaining the differences between the prior art and the claims at issue. 3) Resolving the level of ordinary skill in the pertinent art. 4) Considering objective evidence present in the application indicating obviousness or unobviousness.

7. Claims 1, 3, 5-13, 14, 16-19, 21-25, 27, 28, and 36-43 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Shionoya *et al.* (1983) in view of O'Hagan *et al.* (1999). Shionoya *et al.* (1983) provide a method for the production of immune responses in a mammal comprising the administration of an admixture comprising an immunogen (e.g., BSA (Examples 1-4), inactivated Meth-A tumor cells (Example 5)) and a plant lectin (e.g., abrin),

wherein said administration results in an immune response that is greater as compared to the immune response in the absence of the adjuvant (e.g., see Tables 2-5 and Examples 1-5). The method discloses the generation of both humoral (e.g., see Examples 1, 2, and 4) and cellular (e.g., see Examples 3 and 5) immune responses. The humoral responses included both IgG and IgM antibody production (e.g., see Example 4). Various formulations, routes of administrations, and ratios of immunogen/adjuvant were also described. This teaching does not disclose intranasal administrations, the detection of antibodies in mucosal secretions, a viral immunogen, or the detection of antibody reactivity by ELISA. However, O'Hagan *et al.* (1999) disclose intranasal immunization protocols employing a viral immunogen (e.g., herpes simplex virus type 2 (HSV-2) glycoprotein D2) and known adjuvants (e.g., LTK63 or MF59) (see Results, pp. 2231-2234, Figures 1 and 2, and Table 1). Antibody titers in various samples (e.g., mucosal secretions) were determined by ELISA. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the MF59 or LTK63 adjuvant in the immunization protocol provided by O'Hagan and colleagues with the abrin adjuvant provided by Shionoya and associates, since the latter adjuvant induces strong humoral and cellular immune responses to various immunogens. Thus, the skilled artisan would reasonably expect the administration of a composition comprising abrin and the HSV-2 gD to induce strong humoral and cell-mediated immune responses against the viral envelope glycoprotein.

Applicants assert that the Office has not provided a sufficient motivation for combining the cited references and that there is no reasonable expectation that a combination of immunogen and lectin would result in an enhanced immune response to the immunogen as compared to immunogen administration alone. Neither of these

arguments are persuasive. In response to Applicants' argument that there is no suggestion to combine the references, the Examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references. *In re Nomiya*, 184 U.S.P.Q. 607 (C.C.P.A. 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin*, 170 U.S.P.Q. 209 (C.C.P.A. 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 U.S.P.Q. 545 (C.C.P.A. 1969). In this case, the prior art clearly teaches that lectins are capable of inducing strong immune responses when utilized as an adjuvant. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the MF59 or LTK63 adjuvant in the immunization protocol provided by O'Hagan and colleagues with the abrin adjuvant provided by Shionoya and associates, since the latter adjuvant induces strong humoral and cellular immune responses to various immunogens. Moreover, there was a reasonable expectation of success since the skilled artisan is simply substituting one adjuvant for another. Thus, the skilled artisan would reasonably expect the administration of a composition comprising abrin and the HSV-2 gD to induce strong humoral and cell-mediated immune responses against the viral envelope glycoprotein.

8. Claims 4 and 34 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Shionoya *et al.* (1983) in view of Carrano *et al.* (1999). The teachings of Shionoya *et al.* (1983) have been set

forth *supra* in paragraph 6. This teaching does not disclose an immunogenic compositions comprising a lectin selected from the group consisting of ML-I, ML-II, ML-III, WGA, or UEA-1. Carrano *et al.* (1999) provide immunogenic compositions comprising a lectin (e.g., wheat germ agglutinin, abrin) (see claims). The inventors state that said lectins are useful for stimulating T and B cell responses. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare an immunogenic composition comprising the immunogen of Shionoya *et al.* (1983) and one of the adjuvants provided by Carrano *et al.* (1999), since this would facilitate the generation of strong immune responses against the immunogen of interest.

Applicants traverse and submit that there is insufficient motivation to combine the references since Carrano *et al.* (1999) is directed toward nucleic acid vaccines whereas the claimed invention is directed toward proteinaceous vaccines. As set forth supra, in response to Applicants' argument that there is no suggestion to combine the references, the Examiner recognizes that references cannot be arbitrarily combined and that there must be some reason why one skilled in the art would be motivated to make the proposed combination of primary and secondary references. *In re Nomiya*, 184 U.S.P.Q. 607 (C.C.P.A. 1975). However, there is no requirement that a motivation to make the modification be expressly articulated. The test for combining references is what the combination of disclosures taken as a whole would suggest to one of ordinary skill in the art. *In re McLaughlin*, 170 U.S.P.Q. 209 (C.C.P.A. 1971). References are evaluated by what they suggest to one versed in the art, rather than by their specific disclosures. *In re Bozek*, 163 U.S.P.Q. 545 (C.C.P.A. 1969). In this case, the nucleic acid vaccine is predicated upon the expression of the immunogen of interest after immunization. The adjuvant which is administered in conjunction with the nucleic acid construct

facilitates the development of strong immune responses against the protein immunogen expressed from this construct. Thus, there is more than sufficient motivation to combine the references.

9. Claim 15 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Shionoya *et al.* (1983) in view of Gough and Platt (1984). The teachings of Shionoya *et al.* (1983) have been set forth *supra* in paragraph 6. This teaching does not disclose an immunogenic compositions comprising two or more lectins. Gough and Platt (1984) provide immunogenic compositions comprising a lectin (e.g., lentil bean lectin, jack bean lectin (con A) (see col. 3, second paragraph). The inventors state that said lectins are useful for stimulating T and B cell mitogenesis. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare an immunogenic composition comprising the immunogen of Shionoya *et al.* (1983) and two or more adjuvants as provided by Shionoya *et al.* (1983) and Gough and Platt (1984), since the presence of multiple lectins would reasonably be expected to increase the adjuvanticity of the formulation and lead to a stronger immune response against the immunogen of interest. Applicants argue that the teachings relied upon fail to teach or suggest each of the claimed limitations. This argument is not deemed to be persuasive for the reasons of record set forth above.

10. Claims 20 and 31 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Shionoya *et al.* (1983) in view of Hodges *et al.* (1995). The teachings of Shionoya *et al.* (1983) have been set forth *supra* in paragraph 6. This teaching does not disclose an immunogenic compositions formulated as a nasal spray or for enteric delivery. However, Hodges *et al.* (1995) provide immunogenic compositions that can be formulated for enteric delivery or nasal

delivery (see col. 13, second paragraph). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare an immunogenic composition comprising the immunogen and adjuvant of Shionoya *et al.* (1983) in a formulation suitable for enteric or nasal administration as taught by Hodges *et al.* (1995) since this would facilitate the delivery of immunogen to other immunologically active sites. Applicants' response did not directly address this rejection.

11. Claim 30 stands rejected under 35 U.S.C. § 103(a) as being unpatentable over Shionoya *et al.* (1983) in view of Friedman *et al.* (1998). The teachings of Shionoya *et al.* (1983) have been set forth *supra* in paragraph 6. This teaching does not disclose an immunogenic formulation comprising a bioadhesive polymer. However, Friedman *et al.* (1998) provides an efficient means for delivering an antigen to the target tissue of interest employing a bioadhesive polymer (e.g., see columns 3-10). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to prepare an immunogenic formulation comprising the immunogen and adjuvant of Shionoya *et al.* (1983) with the bioadhesive polymer of Friedman *et al.* (1998) since this would facilitate the long-term delivery of immunogen to the site of interest. Applicants' response did not directly address this rejection.

Allowable Subject Matter

12. The utilization of the plant lectins ML-I, -II, -III, and UEA as mucosal adjuvants appears to be novel and unobvious. Appropriately drafted claim language directed toward immunization methods involving the mucosal administration of these adjuvants in conjunction with a suitable immunogen would be acceptable.

Finality of Office Action

13. Applicants' amendment necessitated any and all new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

14. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward the following Group 1600 fax number: (703) 872-9306. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, Laurie Scheiner or James Housel, can be reached at (703) 308-1122 or (703) 308-4027, respectively. Any inquiry of a general nature or relating to the

status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

08 January, 2004

James C. Housel 1/12/04

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
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